CNTVac: Intranasal HIV-1 mRNA Vaccine Using Carbon Nanotubes (CNTs)

Analysis of the Failures in Distribution Equity of the COVID-19 Vaccine in the US

A Thesis Prospectus
In STS 4500

Presented to
The Faculty of the
School of Engineering and Applied Science
University of Virginia
In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science in Biomedical Engineering

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October 27, 2023

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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Introduction

By the end of 2021, almost 1.2 million people in the US alone had human immunodeficiency virus 1, HIV-1, with only 87% of that number being aware of their condition. In 2021 in the US, 36,136 new cases were diagnosed, with the annual diagnostic rate going up by 7% from 2017 to 2021. HIV-1 disproportionately affects certain US populations, with 40% of new HIV diagnoses among the African American population, 29% of diagnoses among the Hispanic American population and only 25% among the White American population ("Basic Statistics", 2023). While there are currently effective methods for HIV prevention and treatment, they require lifelong commitment and African Americans face many barriers in access to treatment and prevention, such as limited access to high-quality health care, housing, and HIV prevention education ("Prevention Challenges", 2023). Due to the inequity in access to prevention and treatment methods for HIV, there is an acute need for a safe and reliable vaccine that can be widely and equitably distributed.

I propose an intranasal HIV-1 vaccine with a stable shelf life and low toxicity to be developed. This will provide a prevention method for HIV-1 that does not require the lifelong commitment of current prevention methods. This will be an mRNA based vaccine, a vaccine method proven to evoke a strong immune response without the risks of other vaccine methods. The mRNA will be delivered using short carbon nanotubes, a nontoxic novel delivery system for vaccines being developed by LunaLabs (Xu et al., 2023). As this technical project is meant to benefit all racial and ethnic populations affected by HIV, understanding the inherent bias in vaccine development is important to make sure the development and distribution of this vaccine does not marginalize certain populations. To develop strategies to avoid this, I will use the STS framework of technological politics to analyze the inherent bias in the COVID-19 vaccine. More

specifically, I will be looking into how the inherent bias and racial inequity in clinical trials led to inequitable distribution of the COVID-19 vaccine among different racial populations in the US. Attending to the technical aspects, while ignoring social aspects, will leave the challenge only partially resolved because while there will be an HIV-1 vaccine, there will be a lack of understanding of how to equitably distribute said vaccine to the populations that most need it.

Because the broader challenge of developing and distributing an HIV-1 vaccine is sociotechnical in nature, it requires attending to both its technical and social aspects. In the next section I will describe in greater detail the two interconnected research proposals previously mentioned: the technical project of developing a safe intranasal mRNA based vaccine using CNTs as the delivery method that only requires one dose and the STS project that examines the inherent bias in the COVID-19 vaccine development that caused marginalization of the communities demonstrating the most need for the vaccine. While working to develop the proposed vaccine, it will be important for me to consider the pitfalls of the COVID-19 vaccine development to best prevent the inherent bias that is possible in the future steps of the HIV vaccine development, so that it can actually serve the populations with the greatest need.

Technical Project Proposal

Human immunodeficiency virus 1 (HIV-1) is a virus that attacks the immune system by destroying CD4 T cells, a type of immune cell, rendering them ineffective in protecting the body (Chen, 2019). Currently, there are no viable HIV-1 vaccines on the market and the only prevention option that exists other than abstinence from and protection during sex is an oral or injectable medication that greatly reduces the risk of contracting HIV (“Prevention”, 2023). While this medication is effective, it must be administered consistently in order to be effective and requires frequent doctor visits and testing while taking it (“Starting and Stopping PrEP”,

2022). A vaccine is an alternative that provides a quicker and more accessible HIV prevention method, however there are certain challenges in developing an effective and safe HIV-1 vaccine.

Conventional vaccine types that are composed of actual viruses that have been weakened, called live-attenuated vaccines, result in ineffective protection against HIV-1 and have a dangerously high risk of causing actual HIV-1 infection (Churchill et al., 2016; Whitney & Ruprecht, 2004). This has more severe implications with HIV-1 than with other viruses, such as the flu. Additionally, due to the variation of the HIV-1 virus types, the human immune system cannot elicit a broad enough response using current methods (Hemelaar, 2013). For our project we are using an mRNA vaccine, as they have been shown to elicit strong immune responses with certain viruses where other vaccine methods have failed (Pardi et al., 2020). However, while vaccines containing mRNA are safer, they need a delivery system in order to affect the immune system. We will be using short carbon nanotubes (CNTs), cylindrical nanostructures composed of carbon atoms, as a novel vaccine delivery approach being developed at Luna Labs, termed NanoVac. CNTs have demonstrated a non-toxic and effective delivery platform as a potential alternative to other conventional vaccine delivery methods (Xu et al., 2022, 2023).

The goal of this technical project is to develop an effective intranasal HIV-1 vaccine candidate. The mRNA we will be using is the mRNA that encodes for a protein that exists externally on the HIV-1 virus. We will optimize the amount of mRNA to be loaded onto the CNTs and test the delivery efficacy and toxicity of the vaccine formulations through cellular studies. The general procedure will be provided by our advisors at LunaLabs and the project will be divided into two subsections, one being completed during each semester of working on this project. The first task is to prepare CNTs of proper size, antigen ratio and surface functionalization molecules for the best HIV-1 mimic. The CNTs will be cut to mimic the size of

the HIV virus, which will cause cells to generate the proper antibodies, and we will validate the size and surface charge of the CNTs. CNTs will be conjugated with polyethylenimine (PEI), a positive functional group, to prepare for bonding to negatively charged mRNA. The PEI-conjugated CNTs will be loaded with different ratios of mRNA. mRNA quantification methods will be used to analyze how much of the intended mRNA was loaded onto the CNTs and the strength of the interaction of the mRNA to the CNTs to determine the optimal CNT formulation.

In order to validate our vaccine formulation, we will perform cellular studies of the optimized CNT vaccine, where we will see how our target cells interact with the prepared CNTs to be able to predict how the vaccine will perform in the body. We will specifically look at how the vaccine formulation interacts with Calu-3 cells, an epithelial submucosal gland cell line in the lungs (Xu et al., 2022), by first growing Calu-3 cells. We will add the CNT formulation to the cells and look at cell health and survival to determine the cytotoxicity of the vaccine. Formulation transfection, the process of delivery of RNA into the cell, will be tested using fluorescence methods. In-vitro translation (IVT), where the cells turn the mRNA on the CNT into the actual target protein, will also be measured through fluorescence to measure the production of protein within the CNT-transfected Calu-3 cells. Through these methods, we hope to formulate a non-toxic and effectively delivered HIV-1 vaccine formula.

STS Project Proposal

On March 11, 2020, the World Health Organization officially declared COVID-19 to be a pandemic. Various biotechnology companies immediately began funding COVID-19 vaccine projects on an accelerated timeline. In December of 2020, the Pfizer COVID-19 vaccine was issued an Emergency Use Authorization by the Food and Drug Administration, with other

companies soon to follow (“Coronavirus”, n.d.). This began the mass vaccination against the COVID-19 pandemic and led to the eventual official end of the pandemic in 2022. While Black populations were disproportionately affected by the COVID-19 pandemic, with a hospitalization rate double the rate of white Americans (Jason et al., 2023), almost all of the studies done in the US on ethnic minority vaccine acceptance and uptake reported that Black populations had significantly lower vaccine uptake and acceptance as compared to the white populations (Abba-Aji et al., 2022). A 2021 study showed that from December 14, 2020 to May 15, 2021, the rate of vaccination among non-Hispanic White persons was 54.6%, while that of non-Hispanic Black populations was a mere 40.7% (Pingali, 2021). These statistics reflect a significant racial disparity in acceptance and administration of the COVID-19 vaccine.

In the CDC’s analysis of the COVID-19 vaccine inequity for racial minority groups, they report that the contributing factors include education, income, and wealth gaps, job access and working conditions, racism and other forms of discrimination, gaps in healthcare access, transportation and neighborhood conditions, and, most importantly, lack of trust as a result of past medical racism and experimentation (“COVID-19 Vaccine Equity”, 2022). While these are all key factors to the failure of the COVID-19 vaccine distribution, they are ignoring the root cause of some of these issues, specifically when looking at the attitudes of racial minorities towards vaccines. The current discourse fails to acknowledge the inherent bias and racism within the technology itself, instead choosing to blame the inequity on the results of this bias, leading to smaller scale solutions that do not get to the root of the problem. Looking at this problem through a deeper lens will allow for full understanding of the underlying reason for these issues and development of larger scale solutions that can work towards eliminating inequity in vaccine distribution.

I argue that the inherent bias of the COVID-19 vaccine technology, the lack of representation by racial and ethnic minorities in clinical trials, is what led to the distrust of the vaccine by those populations, and therefore their lower rates of vaccination. I will draw on the science, technology, and society (STS) concept of technological politics to guide my analysis of the mass COVID-19 vaccination outcomes. The theory of technological politics, developed by Langdon Winner, states that technological artifacts have inherent politics, or "arrangements of power and authority in human associations" (Winner, 1978, p. 123), that serve to promote certain groups' power while marginalizing and even harming other groups. Winner discusses that a technology's politics can be either intentional, expressing explicit bias, or unintentional, expreccing implicit bias, but either way will have the same effect. In order to support my argument, I will use studies from the CDC, FDA and the actual vaccine companies that report on the racial distribution of clinical trial participants as well as reports on attitudes of different racial and ethnic groups towards the COVID-19 vaccine.

Conclusion

The deliverable for the previously discussed technical problem will be an intranasal HIV-1 mRNA vaccine formulation with CNTs as the delivery vehicle to be used for animal testing, with studies showing the efficiency and safety of delivery. The STS research paper will work to analyze the issues in the development of the COVID-19 vaccine that led to its inherent bias against certain populations, using the framework of technological politics. The results of the technical and STS reports will work to address the issues of access to prevention methods for HIV-1 for the most affected populations by the virus. Looking at the full sociotechnical context of the development of this new HIV-1 vaccine will allow for it to be most beneficial to those who need it most.

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